TO STUDY RANDOM BLOOD SUGAR LEVEL AS A PROGNOSTIC FACTOR IN MODERATE AND SEVERE TRAUMATIC BRAIN INJURY

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DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled "**RANDOM BLOOD SUGAR LEVEL AS A PROGNOSTIC FACTOR IN MODERATE AND SEVERE TRAUMATIC BRAIN INJURY** " submitted towards partial fulfillment of the requirements for the award of **M.Ch. in Neurosurgery** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Ashwani K Chaudhary**, Professor & Head, Department of Neurosurgery, **Dr. Shivender Sobti**, Professor, Department of Neurosurgery. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my Family

&

Teachers

LIST OF ABBREVIATIONS

ARDS	Acute respiratory distress syndrome
BBB	Blood brain barrier
DM	Diabetes mellitus
DH	Diabetic hyperglycemia
FFA	Free fatty acid
GCS	Glasgow coma scale
GFAP	Glial fibrillary acidic protein
GLT	Glutamate transporter
GLAT	Glutamate aspartate transporter
GOS	Glasgow outcome score
HbA1c	Glycosylated haemoglobin
IDDM	Insulin dependent diabetes mellitus
LPR	Lactate pyruvate ratio
PH	Persistent hyperglycemia
RBS	Random blood sugar
RTA	Road traffic accident
SIH	Stress induced hyperglycemia
SIS	Systemic inflammatory syndrome
TBI	Traumatic brain injury
TCA	Tricarboxylic acid
VAP	Ventilator associated pneumonia

ABSTRACT

INTRODUCTION-Head trauma is a major cause of death, disability and public health problems. Damage induced by TBI is divided into 2 types-(1-Primary injury is initiated by a physical insult to the head, resulting in compression and shearing of adjacent tissues. (2-Secondary injuries are complex process that occurs in the hours and days following primary injury, which encompass cranial and systemic complications. Cranial complication may include cerebral edema, intracranial HTN, infection, calcium ion toxicity and vasospasm. Systemic complication are mainly ischemic in nature, and include hypoxemia, hypotension, hypertension, hyperglycemia and hypoglycaemia. Among these secondary complications, hyperglycemia in TBI pt is one of the most common, and correlate the severity of injury and clinical outcome.

AIMS & OBJECTIVES: To evaluate the role of RBS levels as a prognostic factor in moderate and severe head injury patients, in non-diabetic patients.

MATERIALS & METHOD: Consecutive sample of 60 patients admitted in department of Neurosurgery, DMCH, Ludhiana as case of moderate to severe head injury were enrolled for prospective and observational study from March 2020 to September 2021.Blood glucose levels of the pts were evaluated by collecting venous sample at admission, at 24 hrs and at 72 hrs of pts stay. Pre-existing diabetic status was ruled out by Glycosylated Hb(HbA1c) levels. Severity of head injury graded using Glasgow coma scale into mild (13-15), moderate (9-12) and severe (3-8).Outcome was determined by Glasgow outcome score (1-5) at the time of discharge from the hospital.

RESULTS: We found that TBI is more commonly seen in young males and most common cause was RSA. The ICU stay in severe traumatic brain injury had a significant correlation with the random blood sugar at admission. Glasgow outcome score in severe traumatic brain injury had a significant correlation with random blood sugar levels at 24 hours of admission. At all the time of presentation higher levels of random blood sugar(RBS) was found in patients with severe traumatic brain injury.

CONCLUSIONS: Hyperglycemia is one of the most common secondary complication in traumatic brain injury. This study accentuates the fact that hyperglycemia can and should be used more frequently as a biomarker for the outcome in traumatic brain injury.

KEYWORDS: Traumatic brain injury, Glasgow outcome score, Random blood sugar level, Glycosylated haemoglobin.

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INTRODUCTION

Traumatic brain injury is a major cause of mortality and disability in the world[1]. Primary brain injury is the physical damage to the brain that occurs during a traumatic event, causing shearing and compression of the surrounding brain tissue. Numerous secondary brain insults occur intracranially and extracranially which result in secondary brain injury. These are mainly ischemic in nature such as Hypotension (systolic blood pressure [SBP]<90mmHg), Hypoxemia (PaO2<60mmHg;O2Saturation<90%), Hypocapnia (PaCO2<35mmHg), Hypercapnia (PaCO2>45mmHg), Hypertension(SBP>160mmHg, or mean arterial pressure >110 mmHg), Anemia (Haemoglobin<100g/L, or haematocrit<0.30), Hyponatremia (serum sodium<142mEq/L), Hyperglycaemia (blood sugar>10mmol/L), Hypoglycaemia (blood sugar <4.6 mmol/L), Hypo-osmolality (plasma osmolality< 290mOsm/Kg H2O), Acid-base disorders (acidemia: pH < 7.35; alkalemia: pH > 7.45), Fever (temperature > 36.5°C) and Hypothermia(temperature<35.5°C)[2,3].

Hyperglycaemia (both peak glucose and persistent hyperglycaemia) in TBI patients is among the most common secondary brain injuries which correlates with the severity of the trauma and prognosis[4,5]. However, several serum and biomarkers such as Glial fibrillary acidic protein (GFAP), S100B, UCHL-1 and S-100B, have been identified that correlate with various pathologies of mild and severe TBI and have been studied extensively to supplement radiological investigations[6-11]. The use of both sensitive and specific biomarkers may serve as cost-effective tools to aid in acute assessment, especially in the absence of risk factors for intracranial injury[12].

TRAUMATIC BRAIN INJURY

Definitions

Traumatic brain injury is caused by an impact to the head from an external force that disrupts physiological function. External forces can

include direct mechanical impact (i.e blunt trauma),acceleration or deceleration associated injury (i.e whiplash),blast injury caused by a pressure wave (i.e. explosion),or penetrating injury (i.e. gunshot).

Severity of TBI can be classified multiple ways. Originally developed to classify levels of consciousness[13], the Glasgow Coma Scale(GCS) has become the most widely used tool to describe TBI severity. The GCS score ranges from 3 to 15: 3-8 indicating severe,9-12 indicating moderate, and 13-15 indicating mild TBI[14]. Alternative criteria based on loss of consciousness and post-traumatic amnesia are also used.Centers for Disease Control and Prevention (CDC), continue to utilize a combination of clinical variables to assess TBI severity(Table 1).

Table1: Classification of Traumatic Brain Injury.

Criteria	Mild	Moderate	Severe
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of consciousness	0-30 min	>30 min but <24 hours	>24 hours
Alteration of Consciousness	0-24 hours	>24 hours	
Post-Traumatic Amnesia	<24 hours	24 hours-7 days	>7 days
Glasgow Coma Scale	13-15	9-12	3-8

MECHANISMS OF HYPERGLYCEMIA AFTER TRAUMATIC BRAIN INJURY

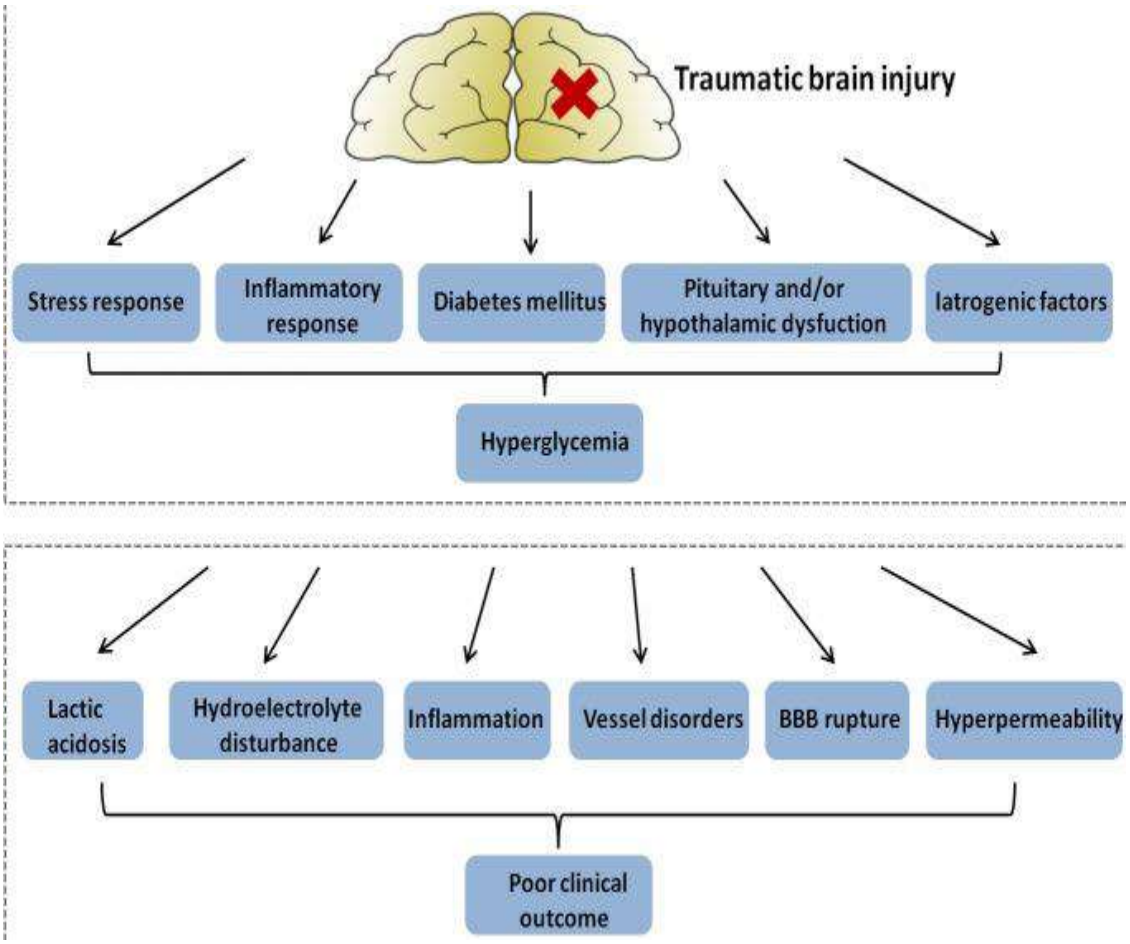

Figure 1: Illustrating hypothetical mechanisms: hyperglycemia in patients with traumatic brain injury (upper panel); and explaining a detrimental effect of hyperglycemia on clinical outcome (lower panel).

There are a number of mechanisms by which hyperglycemia is induced following TBI-

Stress response

There are several explanations for high glucose levels after TBI, and one of the most studied is stress-induced hyperglycemia. During TBI, the hypothalamic-pituitary-adrenal axis and the sympathetic autonomic nervous system are activated, resulting in increased levels of neuro-hormonal factors and insulin resistance. First, the increased levels of stress hormones may influence glycemic levels. After TBI, the activation of the hypothalamic-pituitary-adrenal axis and the

sympathetic autonomic nervous system induce elevated blood levels of catecholamine, cortisol, glucagon and growth hormone, which enhance glycogenolysis and hypermetabolism and lead to excessive glucose production[15,16]. By functioning on islet beta cells' alpha 2 receptor, catecholamines also increase glucagon production and decrease insulin secretion[17,18]. Second, transient insulin resistance (IR) is another mechanism by which stress hormones may affect glucose metabolism. Several reports have demonstrated that TBI reduces insulin sensitivity and secretion, contributing to IR and glucose homeostasis impairment[19]. The released catecholamines can inhibit glucose transport *via* inhibition of insulin binding, leading to IR with hyperinsulinemia[20].

Inflammatory response

TBI is accompanied by a systemic inflammatory response syndrome (SIRS), in which there may be two mechanisms that lead to hyperglycemia. First, during the inflammatory response, several cytokines are released, including TNF-α, IL-6, and CD11d[21]. Studies demonstrated that TNF-α regulated quantity and function of glucose by decreasing levels of adipocyte-specific genes and increasing levels of preadipocyte-specific genes, contributing to insulin resistance and hyperglycemia[22]Second, inflammatory responses increase the level of corticotrophin-releasing hormone (CRH) and stimulate the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary, which induce elevated levels of blood glucose. Nitric oxide (NO), which is activated in the inflammatory response, participates in signal transduction pathways that lead to the release of corticosterone from the adrenal gland, and finally results in hyperglycemia[23].

Diabetes mellitus (DM)

Diabetes mellitus (DM) is another source of hyperglycemia in this setting. Severe TBI with DM has a higher mortality (14%) compared to severe TBI without DM (8.2%), and TBI with insulin-dependent DM (IDDM) has a higher mortality rate (17.1%) than patients without

insulin-dependent DM (NIDDM). These results indicate that insulin deficiency may contribute to the increased mortality after TBI, and DM has the potential to be an independent predictor of poor outcome and mortality after TBI[24,25]. Latent diabetes mellitus may be particularly problematic, especially in elderly patients. The symptoms of DM can be exacerbated after severe TBI, and undiagnosed DM may contribute to insulin resistance without characteristic clinical symptoms[26].

Pituitary and hypothalamic dysfunction

Pituitary and/or hypothalamic dysfunction following TBI is a significant occurrence that is rarely considered by clinicians. Recently, this topic has attracted some attention owing to high prevalence of pituitary or hypothalamic dysfunction after moderate-severe TBI and its association with increased morbidity and poor recovery[27]. In addition to its role in regulating the stress response, the hypothalamus-pituitary axis is vital for balancing glucose homeostasis, acting to decrease hepatic gluconeogenesis and increase insulin sensitivity[28]. Pituitary dysfunction directly leads to impaired glucose metabolism and may act as a potential cause of hyperglycemia[29]. In addition, injury of the pituitary leads to disorders of neuroendocrine function[30,31], and, amongst these, deficiency of gonadotrophic hormones and growth hormones are commonly induced by TBI and may result in an imbalance of glucose metabolism[32]. Thus, pituitary/hypothalamic dysfunction may contribute significantly to hyperglycemia in TBI patients.

Iatrogenic factors

There are several other explanations of hyperglycemia induced by TBI. Surgery,anaesthesia, treatment strategies (including too high a dosage of hyperosmotic glucose or a high calorie substance), and psychological factors, may also lead to hyperglycemia in TBI patients, especially in severe TBI[33,34].

HYPERGLYCEMIA AND CLINICAL OUTCOMES AFTER TRAUMATIC BRAIN INJURY

There are a number of ways by which hyperglycemia may increase the damage of nerve function and brain structure.

Lactic acidosis

In the early stages after severe TBI, local blood flow decreases[35]. During ischemic and hypoxic conditions, hyperglycemia inhibits the tricarboxylic acid cycle (TCA) and promotes anaerobic glycolysis, contributing to the accumulation of lactic acid and disturbance of pH homeostasis. In support of a detrimental function of lactic acid is the discovery that in patients with severe TBI, hyperglycemia is associated with both intracellular acidosis and disruption of BBB, eventually leading to ischemia, edema and necrosis[36,37]. Additionally, injured nerve cells cannot metabolize the excess glucose using the mitochondrial aerobic metabolic pathway, causing general decreased glucose utilization[38]. Finally, severe TBI or a reduced blood supply leads to increased metabolism of local brain tissues further stimulating glycolysis[39]. The above pathways promote accumulation of lactic acid and eventually contribute to dysfunctional energy metabolism in nerve cells.

Electrolyte disturbances

Within minutes after TBI, dysfunctional energy metabolism and lactic acidosis lead to increased intracellular Ca^{2+}, causing cellular toxicity and the accumulation of free fatty acid (FFA) and glutamate[40,41]. Excessive glutamate promotes increased Na^{+} and Ca^{2+} to enter into cells, and the resulting intracellular Ca^{2+} overload stimulates cell damage *via*caspaseactivation[42]. As astrocytes represent the main defense by absorbing glutamate, an initial glutamate excitotoxicity occurs in neurons[43]. However, during the secondary injury stage, if extracellular glutamate levels are constantly increased, the expression of glutamate transporters (glutamate transporter-1, GLT-1) and the glutamate-aspartate transporter (GLAST) decreases, and the intracellular Na^{+} can reverse transport. This event favors the release of

glutamate from astrocytes rather than neurons, and the astrocytes actually enhance glutamate excitotoxicity[44,45]. Additionally, a relatively large amount of lactic acid leads to reduced ATP and impairs the Na^+-K^+-ATPase causing excessive extracellular Na^+ levels and cell edema that ultimately results in intracranial hypertension and cerebral hernia[46].

Inflammation

Hyperglycemia after severe TBI is associated with an increase in pro-inflammatory cytokines and pro-inflammatory transcription factors, such as transforming growth factor (TGF-β), interleukin 1β (IL1-β) andtumor necrosis factor-α (TNFα)[47,48]. These cytokines increase significantly in the peripheral blood, cerebrospinal fluid, and brain tissue after TBI, which closely correlates with the severity and bad outcome of TBI patients[49]. An *in vitro* experiment demonstrated that hyperglycemia induced by walnut oil increased the release of pro-inflammatory cytokines, which led to reduced antioxidant capacity and oxidative DNA damage of human monocytic cells (U937)[50]. Furthermore, microglia activation and endothelial cell damage induced by inflammation after TBI could lead to brain injuries, such as edema[51]. Therefore, cytokines play an important role in the neuropathology of TBI, and inhibition of these cytokines indeed had a correlation with neuroprotective effects after TBI, especially the improvement of brain edema and neurological outcomes[52].

Other effects

Hyperglycemia can affect clinical outcomes in other ways. For instance, hyperglycemia can directly cause increased blood viscosity and diffuse small vessel disorders, resulting in ischemia and hypoxia in the brain tissues[53].

Cerebral hypoxia and ischemia results in a significant increase in the lactate: pyruvate ratio (LPR). A LPR > 20-25 is a threshold for cerebral ischemia which is associated with poor outcome in TBI.26 Hyperglycaemia sets in neuronal death by releasing extracellular zinc

and neuronal NADPH oxidase activation. This is also accompanied with an increase in pro-inflammatory cytokines and pro inflammatory transcription factors. Hyperglycemia may accelerate cerebral vasospasm. Additionally, hyperglycemia exacerbates edema of endothelial cells, impairs glial cells, and can induce the rupture of the BBB[54,55]. Hyperglycemia also has the potential to accelerate cerebral vasospasm[56]. Thus, the causal relationship between hyperglycemia and poor clinical outcome in TBI patients may be multifactorial. In the sequence of insults that occur after TBI, hyperglycemia may play a detrimental role by elevating secondary complications such as dysregulated energy metabolism, infection, intracranial edema, and intracranial hypertension

In conclusion, an elevated stress and inflammatory response seem to be the major causes of hyperglycemia after TBI. Preexisting hyperglycemia does not seem to have a predominant role in TBI patients, and a relationship between pituitary and/or hypothalamic dysfunction, iatrogenic factors, and hyperglycemia is plausible. This study was planned to evaluate the role of random blood glucose levels as a prognostic factor in moderate and severe head injury patients in non-diabetic patients.

AIMS AND OBJECTIVES

To evaluate the role of random blood glucose levels as a prognostic factor in moderate and severe traumatic brain injury in non diabetic patients.

REVIEW OF LITERATURE

In a study by Kafaki et al about 39% (*n* = 85) of patients were admitted with hyperglycemia during the study period. The mortality rate in patients with glucose >200 mg/dL was 65.8% (*N* = 56), against 23.7% (*N* = 32) in the group with glucose < 200 mg/dL, with mortality rising as the blood glucose level increased (*P* = 0.014)[57].

In a study by Vikul Kumar et al 216 pt were included, the mean glucose level at admission in case of mild TBI was 70.5±9.08 and 24hrs after injury it was 82.94±18.3. In case of moderate TBI the mean glucose values were 79.93±9.18 and 93.72±10.44 respectively. Severe TBI showed glucose at admission 105.67±23.81 and higher 24 hrs later, 128.02±23.99. Higher mean glucose level at admission and 24 hrs after injury was associated witha poor outcomes in these pts with isolated TBI.

Young and associates looked at 59 consecutive brain injured pts until 18 days after admission. All had a max. GCS of 4-10 in the first 24 hrs and attempted to maintain blood glucose to a level <200 mg/dl. They found that pts with the highest peak admission glucose had the worst neurologic outcomes. There was a significant GCS improvement over the 18-day period in pts with a blood glucose <200mg/dl compared to those with a blood glucose level of >200 mg/dl[58].

Sung and colleagues prospectively studied admission glucose and outcome in pts admitted to the trauma icu using 200 mg/dl as the critical blood glucose value. Pts with blood glucose concentration >200 mg/dl had a significantly increased number of ventilator days and length of stay, as well as increased infection and mortality rates[59].

Van Beek et al. correlated admission glucose levels to 6-month outcomes in nearly 5000 patients from six phase third trials entered into the IMPACT (InternationalMission for Prognosis and Analysis of Clinical Trials in TBI) database, and found a significant association with increasing levels of admission blood glucose and poor outcomes[60].

In a study by UshaAdiga et al in 2012 Random Blood Sugar(RBS) was 189.93 ± 51.74 mg/dl in patients and 106.47±18.32 mg/dl in healthy controls. Blood sugar is significantly elevated in TBI patients compared to controls (P<0.0001). GCS of patients ranged from 3-14. Correlation study showed that Glasgow coma scale bears a strong negative correlation(r= - 0.7043) with blood sugar which is statistically significant (p<0.05). This implies that higher the Random Blood Sugar, worse is the patient's status of consciousness and vice versa[61].

In a study in 2015 by JavaherKhajavikhanetal about 34(40%) of patients were admitted with hyperglycaemia (RBS ≥ 200 mg/dl) over the study period. The mortality rate, length of ICU stay, hospital stay, ISS and VAP & ARDS in patients with RBS levels ≥ 200 mg was significantly higher than patients with RBS levels below ≤ 200mg (p<0.05, p<0.001). A significant correlation was found between RBS with GCS arrival, length of ICU stay, length of hospital stay, ISS, mechanical ventilation and VAP & ARDS (p<0.05, p< 0.001). RBS is a predicate factor for ISS (p <0.05, OR : 1.36), GCS (p <0.001, OR : 1.69), mechanical ventilation (p< 0.05, OR : 1.27), VAP & ARDS (p <0.001, OR : 1.68), length of ICU stay (p <0.001, OR : 1.87) and length of hospital stay (p <0.05, OR : 1.24)[62].

Adeolu, et al conducted a study in the Nigerian population in the year 2015 in which there were 146 male and 30 female patients (range: 2 years to 78 years; mean;34.4 years, SD: 16.4 years). Most (36.4%) of the patients had severe HI. Only 2.5% of the patients had hyperglycaemia at admission. Death occurred in 25% of the patients, moderate disability occurred in 30.1% and good outcome occurred in 35.8%. Hyperglycaemia occurred in one patient each in mild and severe head injuries and in two patients with moderate head injury. All the patients with hyperglycaemia had favourableoutcomes[63].

Danisman et al conducted a study in which the median age of the study population was 7 years and the median GCS was 11. There was a significant negative correlation between blood glucose level and GCS (p < 0.05). A significant correlation in the negative direction was observed between GCS and blood glucose level (r = −0.658, p < 0.05).

Seventy-seven percent of the patients were admitted to hospital, while 6% died in ED[64].

In a study by Torbati et al as the SCI tauma was more severe, the blood sugar level inceases with a higher rate. Besides, there was a significant difference (p =0.001) in MF of patients before and after the insulin protocol prescription n neurosurgical patients is known to correlate highly with progression of prior imaging abnormalities and also new pathology. This has been demonstrated in unselected neurosurgical patients traumatic brain injury (TBI), vascular pathology, and in the postoperative period. When neurological deterioration is not verifiable—for example, as in the case of a patient with poor results on baseline examination or under sedation—the value of routine imaging has also been demonstrated, with detection of new pathology and worsening of preexistingfindings[65].

LiuDeRyke*et al*. demonstrated that peak random blood sugar within the first twenty four hours of injury and admission has the best prognostic value in predicting outcome[66].

Miller et al., found the impact of severity of brain trauma on blood sugar increasing rate[67].

Marton in children found that hyperglycemia with in the first 24 hrs of TBI was highly a/w poor outcome[68].

During one study by Rovilias A and Kotsou S, a total of 267 patients with moderate or severe TBI (GCS scores 3-12) were admitted. Patients with severe TBI had significantly higher glucose levels than those with moderate injury. Furthermore, patients who subsequently had an unfavorable outcome had higher glucose levels (>200 mg/dL or>11mmol/L) than did those with a better prognosis[69]. In addition, the relationship between high blood glucose levels and poor outcome after TBI appears to be more pronounced with persistent hyperglycemia (PH) than solely hyperglycemia on admission[70].

One study found that persistent hyperglycemia, defined as average dailyblood glucose level > 149 mg/dl for the first week after injury, was associated with five fold increase in mortality in a cohort of 834 patients with severe TBI[71,72].

Jeremitsky et al. study showed that early hyperglycemia in severe trauma patients' associated with poor outcomes and tight glucose control is needed to achieve better outcomes and prognosis[73].

Hyperglycemia worsens cerebrospinal and renal damages since it cause ischemia (insufficient blood supply), hypophosphatemia (serum phosphate reduction), gastro paresis (delayed gastric emptying), delayed wound healing, and white blood cells dysfunctions[74]. The results of conducted survey showed that controlling BS level in traumatic brain injury patients leads to faster restoration of consciousness and better outcomes.

In a study done by Kreutziger J et al, 555 patients were stratified according to admission blood glucose concentration to one of five groups: group 1 (n=35) blood glucose <5.56 mmol/L; group 2 (n=205) blood glucose 5.56-7.7 mmol/L; group 3 (n=173) blood glucose 7.5-10.0 mmol/L; group 4 (n=111) blood glucose 10.0-15.0 mmol/L; and finally group 5 (n=31) blood glucose >15.0 mmol/L. In total, 103 of the 555 died. Mortality was significantly higher in those with the highest blood glucose (groups 3-5). Less than 8 % of those in groups 1 and 2 died; this compared with 17 % in group 3, 38 % in group 4 and 74 % in group 5[75].

In a prospective cohort study by Salim et al, 2009., involving 834 patients with severe TBI, it was found that persistent hyperglycemia (defined as average daily blood glucose levels greater than 149 mg/dl for the first week after injury), was associated with a four-fold increase in mortality. According to Walia&Sutcliffe(2002), hyperglycemia was more strongly predictive of the outcome of 338 patients with head injury compared to mean arterial blood pressures[72].

In 2007, Scalea and colleagues14 evaluated the impact of a tight glucose control regimen on outcome in critically injured trauma patients. Their experimental protocol included a 24-month period without strict blood glucose control (pre intervention group) compared to a subsequent 24-month period with strict glycemic control (post intervention group). Similar to the previous studies by Bochicchio and

associates, glucose levels were stratified into low (≤150 mg/dl), medium (150–219 mg/dl), and high (≥220 mg/dl). The patients were further stratified into six blood glucose categories: all low, all moderate, all high, improving, worsening, and highly variable. In the post intervention phase, a strict insulin protocol was instituted with a target blood glucose level of 100– 150 mg/dl. Mortality was significantly higher in the high, worsening, and highly variable groups during both time periods[76].

During a 4-year study by Bosarge PL et al, a total of 626 patients were enrolled with severe TBI defined by GCS score from 3 to 8. Among 184 patients admitted with hyperglycemia, 152 (82.6%) were diagnosed with stress-induced hyperglycemia (SIH) and 32 patients (17.4%) were diagnosed with diabetic hyperglycemia (DH). Patients with SIH had a 50% increased mortality as compared to nondiabetichyperglycemia patients, whereas DH patients did not have a significant increase in mortality[77].

According to some studies have shown that malnutrition is associated with a higher mortality rate in severe TBI patients, and early effective nutritional support can improve insulin resistance and patient prognosis[78]. Insulin increases glucose utilization and decreases the damage of hyperglycemia to brain cells[79]. A slightly higher blood glucose (5-8mmol/L) seems to be favourable during the first week while lower blood glucose (3.5-6.5 mmol/L) may be more favourable during the later stages of recovery during a randomized controlled study in patients with severe TBI[80].

According to Galgano et al. 2017, Hyperglycemia can worsen the underlying brain damage by causing free radical injury, apoptosis and tissue lactic acidosis. Whereas efforts are made to prevent and manage the primary brain injury, secondary brain injury is often overlooked culminating in a “second hit phenomenon”.

MATERIAL AND METHODS

Place of study-This study was conducted in Department of Neurosurgery, Dayanand Medical College and Hospital (DMCH), Ludhiana.

Type of study- Prospective and Observational study.

Duration of study-March 2020 to September 2021

Sample size-Consecutive sample of 60 patients admitted as case of moderate or severe head injury enrolled for study.

Inclusion and Exclusion criteria-

Inclusion criteria-

Sixty consecutive patients admitted as case of moderate or severe traumatic brain injury.

Exclusion criteria-

1. Pre-existing diabetic status
2. Pre-existing comorbidities.
3. Pre-existing metabolic disorders like liver pathologies.
4. Polytrauma patients

METHDOLOGY

This study is a prospective and observational study of all moderate and severe traumatic brain injuries admitted at Neurosurgery Department, DMCH during March 2020 to September 2021 time period. Glucose levels of the patients were evaluated by collecting venous samples at admission, at 24 hrs and at 72 hrs of stay. Patients pre-existing diabetic status was ruled out by HbA1c levels. Data on mortality, ICU length of stay, hospital length of stay, admission GCS score,requirement of mechanical ventilation was collected. Severity of head injury graded using Glasgow coma scale into mild (13-15),

moderate (9-12) and severe (3-8).Outcome was determined by Glasgow outcome score(1-5) at the time of discharge from the hospital.

GLASGOW OUTCOME SCORE

The Glasgow Outcome Score applies to patients with brain damage allowing the objective assessment of their recovery in five categories. This allows a prediction of the long-term course of rehabilitation to return to work and everyday life

Table 2: Glasgow Outcome Score.

1. Death	Severe injury or death without recovery of consciousness
2. Persistent vegetative state	Severe damage with prolonged state of unresponsiveness and a lack of higher mental functions
3. Severe disability	Severe injury with permanent need for help with daily living
4. Moderate disability	No need for assistance in everyday life, employment is possible but may require special equipment.
5. Good outcome	Light damage with minor neurological and psychological deficits.

STATISTICAL ANALYSIS

Data described in terms ofrange; mean ± standard deviation (±SD),median, frequencies (number of cases) and relative frequencies(percentages) as appropriate. For comparing categorical data, Chi square (x^2) test was performed and exact test was used when the expected frequency was less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft windows.

OBSERVATION & RESULTS

Table 3: Socio-demographics of the sample population.

		TBI				Total	Chi-square value	p-value
		Moderate		Severe				
Age group	1(<40 yrs)	20	63%	20	71%	40	2.970	0.224
	2(41-50 yrs)	11	34%	5	18%	16		
	3(>50 yrs)	1	3%	3	11%	4		
Total		32	100%	28	100%	60		

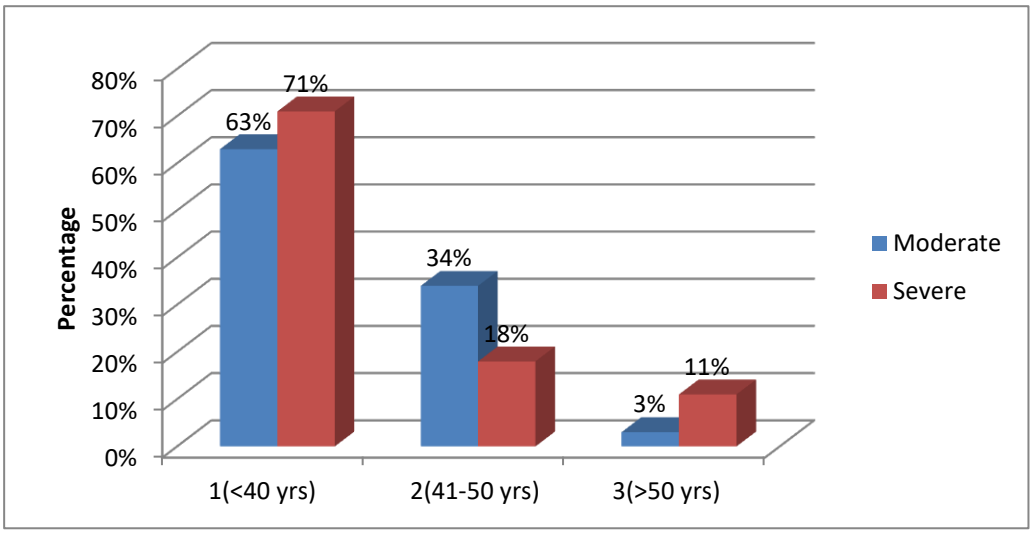

Figure 2: Moderate and severe traumatic brain injury in various age group.

Table 4: Male Female ratio in moderate and severe traumatic brain injury.

		TBI				Total	Chi-square value	p-value
		Moderate		Severe				
Sex	F	6	19%	2	7%	8	1.741	0.264
	M	26	81%	26	93%	52		
Total		32	100%	28	100%	60		

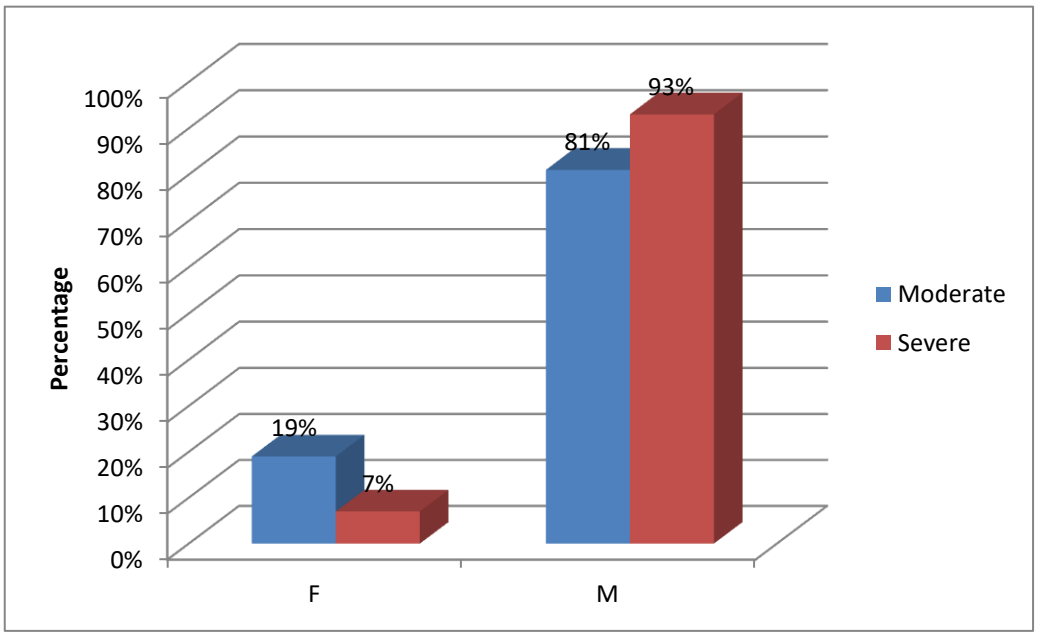

Figure 3: Male Female ratio in moderate and severe traumatic brain injury.

Table 5: RBS level in moderate and severe traumatic brain injury.

		TBI				Total	Chi-square value	p-value
		Moderate		Severe				
RBS 1	< 100	5	16%	2	7%	7	5.328	0.149
	101-150	21	66%	15	54%	36		
	151-200	6	19%	8	29%	14		
	> 200	0	0%	3	11%	3		
RBS 24	< 100	3	9%	1	4%	4	3.080	0.379
	101-150	26	81%	22	79%	48		
	151-200	3	9%	3	11%	6		
	> 200	0	0%	2	7%	2		
RBS 72	< 100	3	9%	2	7%	5	0.577	0.749
	101-150	28	88%	24	86%	52		
	151-200	1	3%	2	7%	3		
Total		32	100%	28	100%	60		

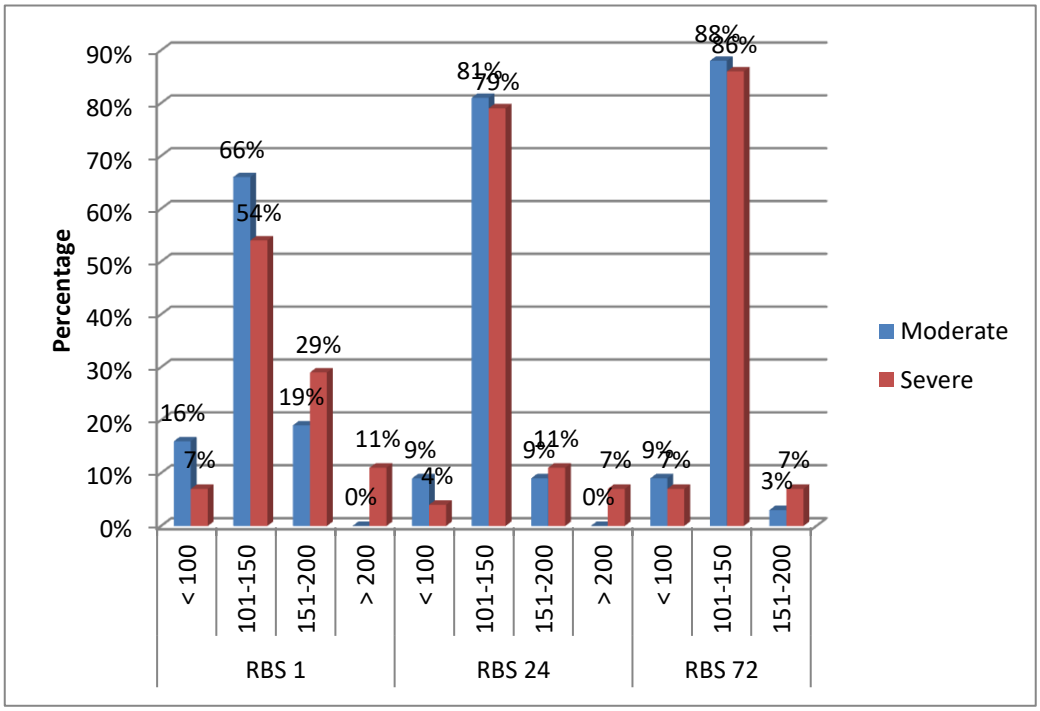

Figure 4: RBS level in moderate and severe traumatic brain injury.

Table 6: Glasgow outcome score in moderate and severe traumatic brain injury.

		TBI				Total	Chi-square value	p-value
		Moderate		Severe				
Glasgow Outcome Score	1	0	0%	1	4%	1	14.686	**0.005**
	2	0	0%	6	21%	6		
	3	0	0%	2	7%	2		
	4	4	13%	6	21%	10		
	5	28	88%	13	46%	41		
Total		32	100%	28	100%	60		

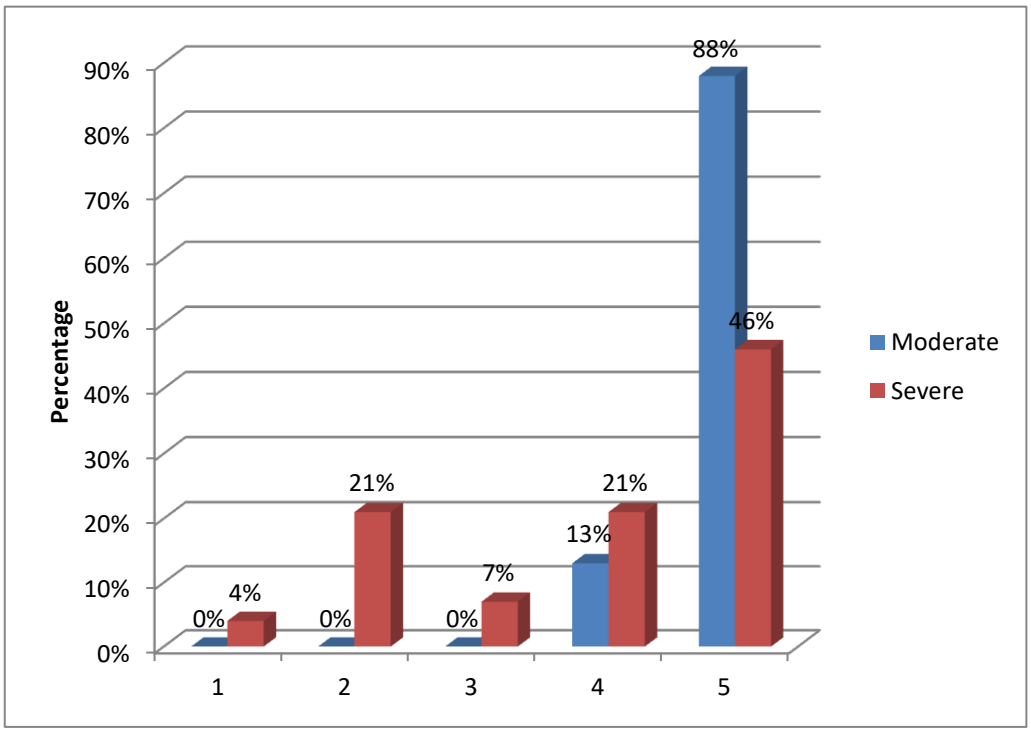

Figure 5: Glasgow outcome score in moderate and severe traumatic brain injury.

Table 7: Mode of injury in moderate and severe traumatic brain injury.

		TBI				Total	Chi-square value	p-value
		Moderate		Severe				
Mode of injury	Assault	1	3%	1	4%	2	5.211	0.391
	Domestic fall	1	3%	0	0%	1		
	Fall from height	0	0%	1	4%	1		
	Rail track accident	0	0%	1	4%	1		
	RSA	30	94%	25	89%	55		
Total		32	100%	28	100%	60		

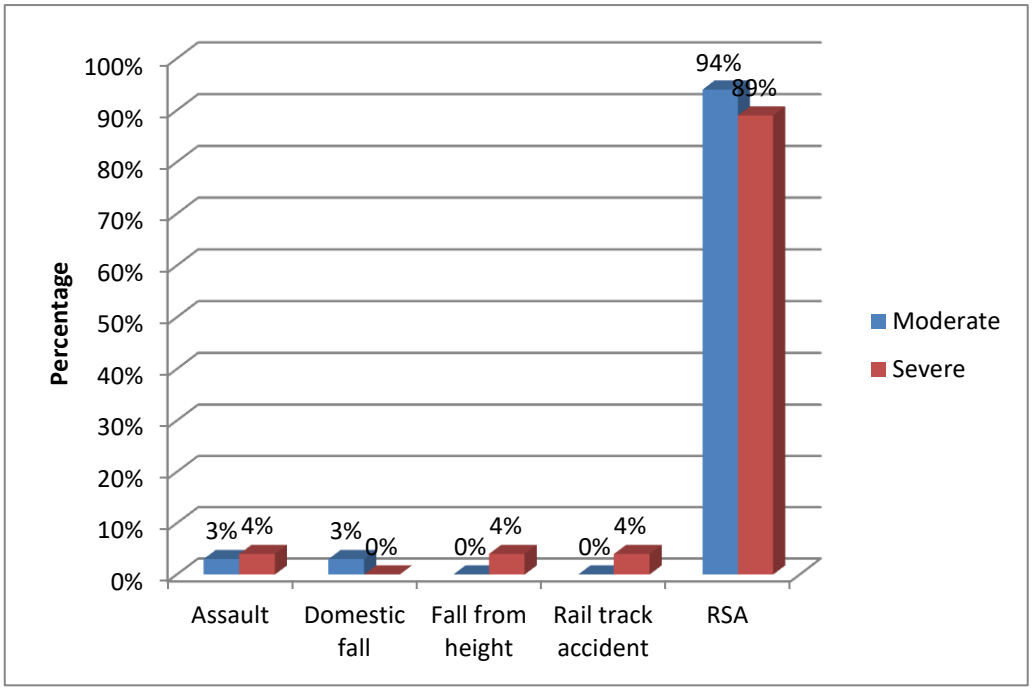

Figure 6: Mode of injury in moderate and severe traumatic brain injury.

Table 8: Mean RBS value with respect to glasgow outcome score in moderate traumatic brain injury.

Moderate	**Glasgow Outcome Score**	N	Mean	sd	Std. Error	Minimum	Maximum	F	p-value
RBS at admission	4	4	126.25	39.18	19.59	100.00	184.00	0.002	0.966
	5	28	125.61	25.98	4.91	77.00	190.00		
	Total	32	125.69	27.14	4.80	77.00	190.00		
RBS at 24 hours	4	4	141.50	37.76	18.88	110.00	196.00	3.926	0.057
	5	28	118.04	19.67	3.72	91.00	182.00		
	Total	32	120.97	23.18	4.10	91.00	196.00		
RBS at 72 hours	4	4	127.00	17.32	8.66	108.00	150.00	1.16	0.29
	5	28	117.86	15.71	2.97	91.00	162.00		
	Total	32	119.00	15.92	2.81	91.00	162.00		

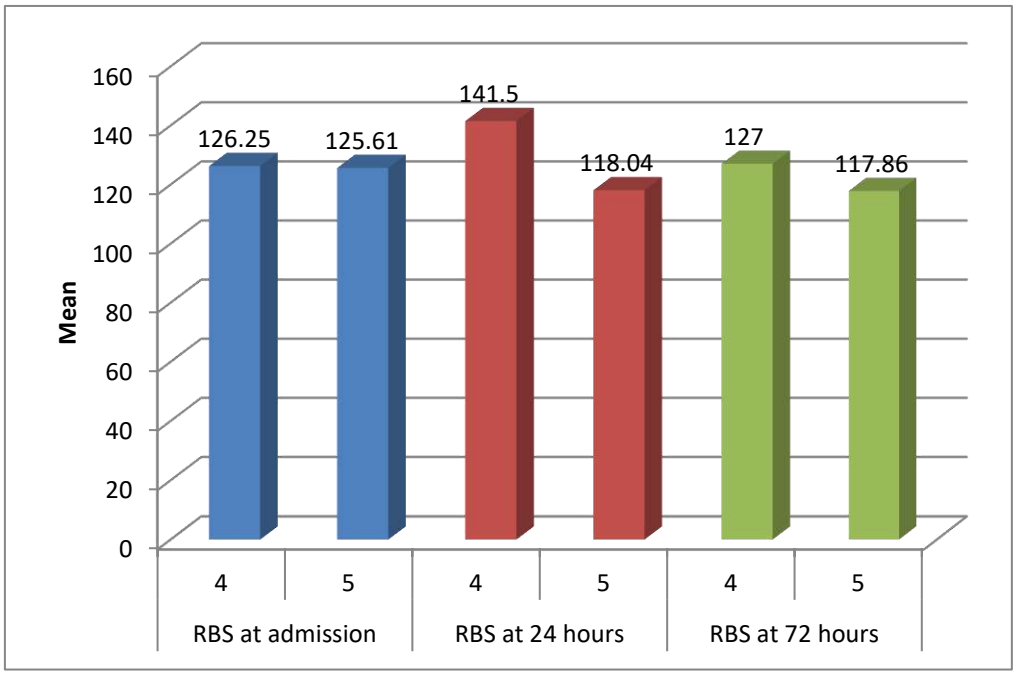

Figure 7: Mean RBS value with respect to glasgow outcome score in moderate traumatic brain injury.

Table 9: Mean RBS value with respect to glasgow outcome score in severe traumatic brain injury.

Severe	**Glasgow Outcome Score**	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	F	p-value
RBS at admission	1	1	198.00	.	.	198.00	198.00	0.362	0.833
	2	6	167.67	55.79	22.78	130.00	275.00		
	3	2	136.50	12.02	8.50	128.00	145.00		
	4	6	154.50	44.39	18.12	87.00	212.00		
	5	13	155.92	46.08	12.78	90.00	270.00		
	Total	28	158.25	44.82	8.47	87.00	275.00		
RBS at 24 hours	1	1	240.00	.	.	240.00	240.00	5.743	**0.002**
	2	6	141.17	37.19	15.18	92.00	201.00		
	3	2	138.50	2.12	1.50	137.00	140.00		
	4	6	125.67	17.72	7.23	113.00	160.00		
	5	13	126.00	19.06	5.29	102.00	170.00		
	Total	28	134.14	30.84	5.83	92.00	240.00		
RBS at 72 hours	1	1	140.00	.	.	140.00	140.00	0.718	0.589
	2	6	123.83	12.72	5.19	108.00	140.00		
	3	2	125.50	41.72	29.50	96.00	155.00		
	4	6	120.67	14.64	5.98	98.00	144.00		
	5	13	114.15	18.85	5.23	101.00	166.00		
	Total	28	119.36	18.12	3.43	96.00	166.00		

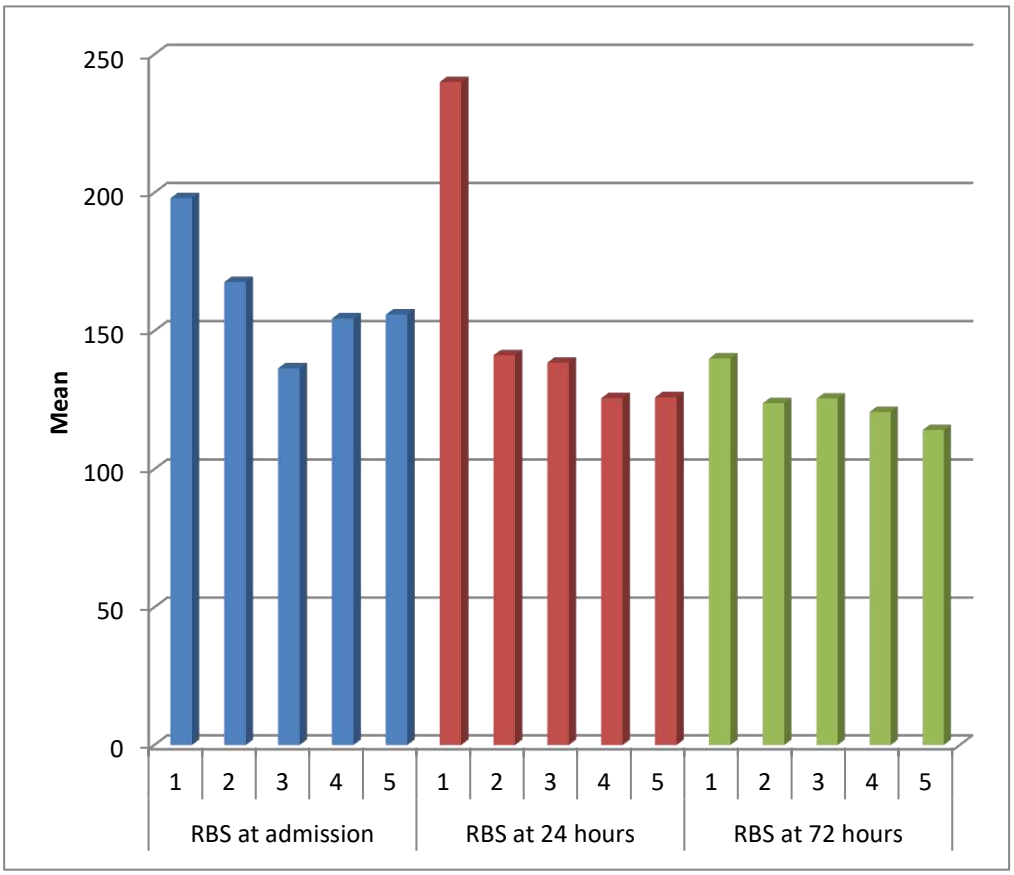

Figure 8: Mean RBS value with respect to glasgow outcome score in severe traumatic brain injury.

Table 10: Mean ICU stay with respect to RBS at admission, 24 hours and 72 hours in moderate traumatic brain injury.

Moderate	ICU stay	N	Mean	Std. Deviation	Std. Error	Min	Max	F	p-value
RBS at admission	< 100	5	3.20	5.63	2.52	0.00	13.00	0.314	0.733
	101-150	21	4.90	4.62	1.01	0.00	15.00		
	151-200	6	5.17	3.60	1.47	0.00	10.00		
	Total	32	4.69	4.52	0.80	0.00	15.00		
RBS at 24 hours	< 100	3	1.67	1.53	0.88	0.00	3.00	1.073	0.355
	101-150	26	4.77	4.76	0.93	0.00	15.00		
	151-200	3	7.00	3.00	1.73	4.00	10.00		
	Total	32	4.69	4.52	0.80	0.00	15.00		
RBS at 72 hours	< 100	3	5.67	0.58	0.33	5.00	6.00	0.556	0.58
	101-150	28	4.43	4.75	0.90	0.00	15.00		
	151-200	1	9.00	.	.	9.00	9.00		
	Total	32	4.69	4.52	0.80	0.00	15.00		

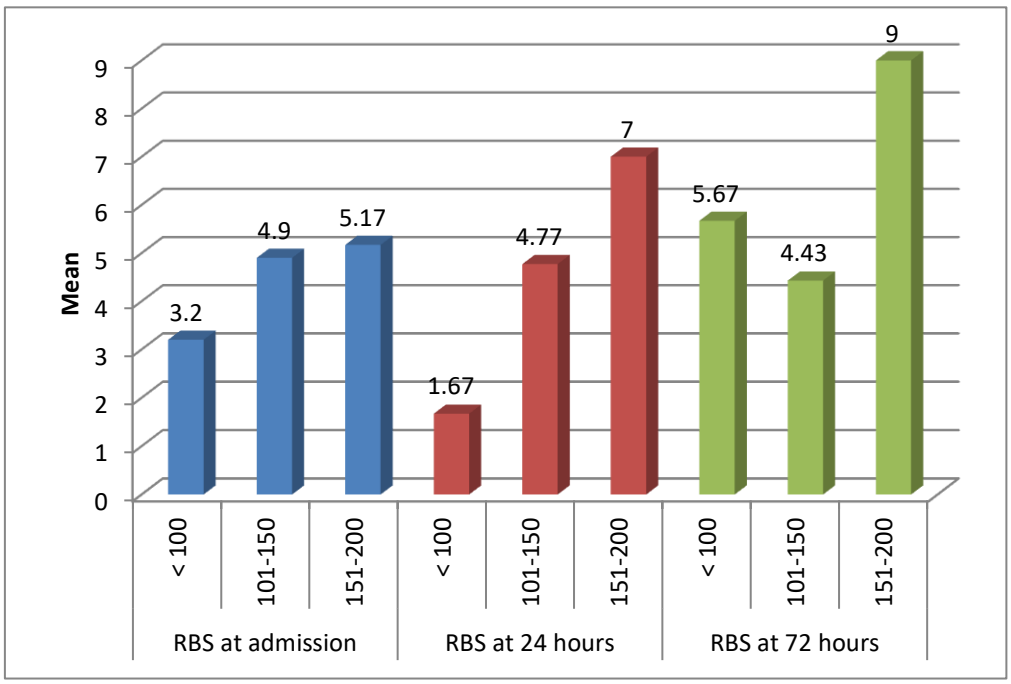

Figure 9: Mean ICU stay with respect to RBS at admission, 24 hours and 72 hours in moderate traumatic brain injury.

Table 11: Mean ICU stay with respect to RBS at admission, 24 hours and 72 hours in severe traumatic brain injury.

Severe	ICU stay	N	Mean	Std. Deviation	Std. Error	Min	Max	F	p-value
RBS at admission	< 100	2	1.50	2.12	1.50	0.00	3.00	3.651	**0.027**
	101-150	15	14.00	7.11	1.84	3.00	28.00		
	151-200	8	8.13	4.09	1.44	4.00	16.00		
	> 200	3	9.33	3.51	2.03	6.00	13.00		
	Total	28	10.93	6.79	1.28	0.00	28.00		
RBS at 24 hours	< 100	1	19.00	.	.	19.00	19.00	1.128	0.357
	101-150	22	10.95	7.12	1.52	0.00	28.00		
	151-200	3	12.33	3.51	2.03	9.00	16.00		
	> 200	2	4.50	0.71	0.50	4.00	5.00		
	Total	28	10.93	6.79	1.28	0.00	28.00		
RBS at 72 hours	< 100	2	12.50	4.95	3.50	9.00	16.00	0.172	0.843
	101-150	24	11.00	7.11	1.45	0.00	28.00		
	151-200	2	8.50	6.36	4.50	4.00	13.00		
	Total	28	10.93	6.79	1.28	0.00	28.00		

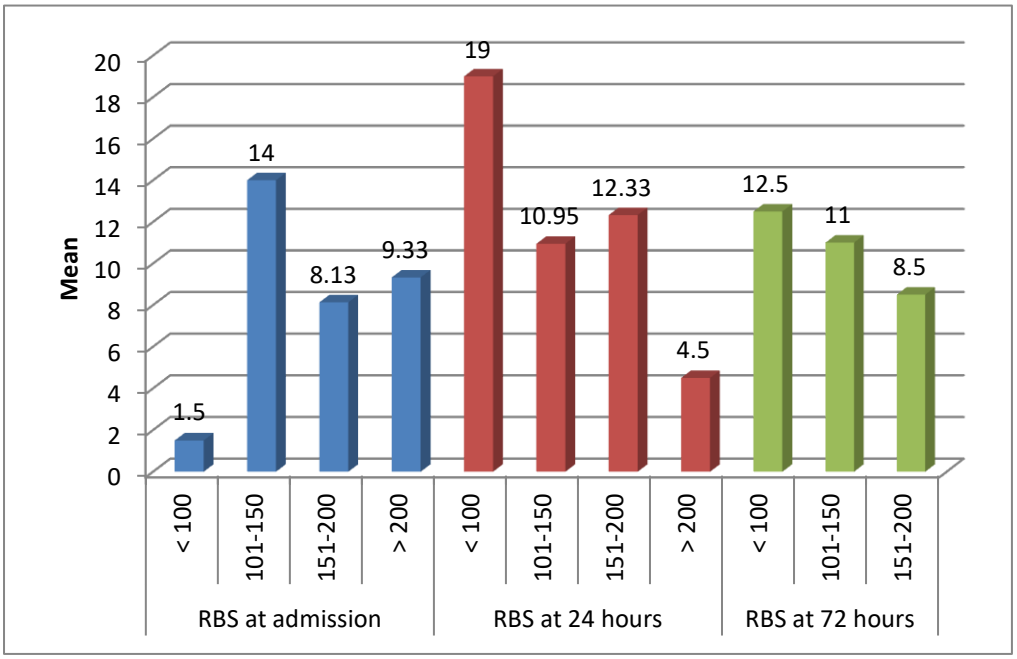

Figure 10: Mean ICU stay with respect to RBS at admission, 24 hours and 72 hours in severe traumatic brain injury.

Table 12: Mean age, hospital stay, ICU stay and HbA1c in moderate and severe traumatic brain injury.

	Moderate		Severe		t	p-value
	Mean	SD	Mean	SD		
Age(yrs)	34.63	10.70	35.54	12.34	-0.306	0.761
Hospital stay	13.19	6.99	26.29	20.45	-3.407	**0.001**
ICU stay	4.69	4.52	10.93	6.79	-4.240	**0.000**
HbA1c	5.23	0.28	5.24	0.35	-0.097	0.923

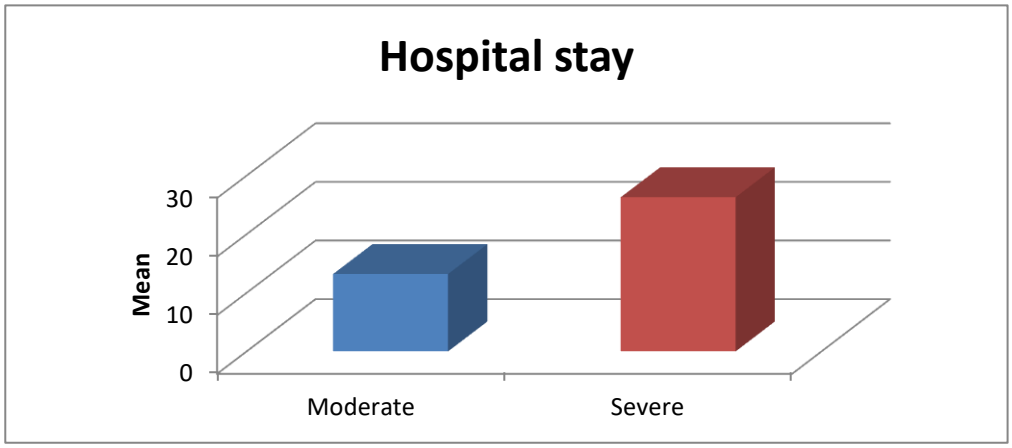

Figure 11: Mean hospital stay in moderate and severe traumatic brain injury.

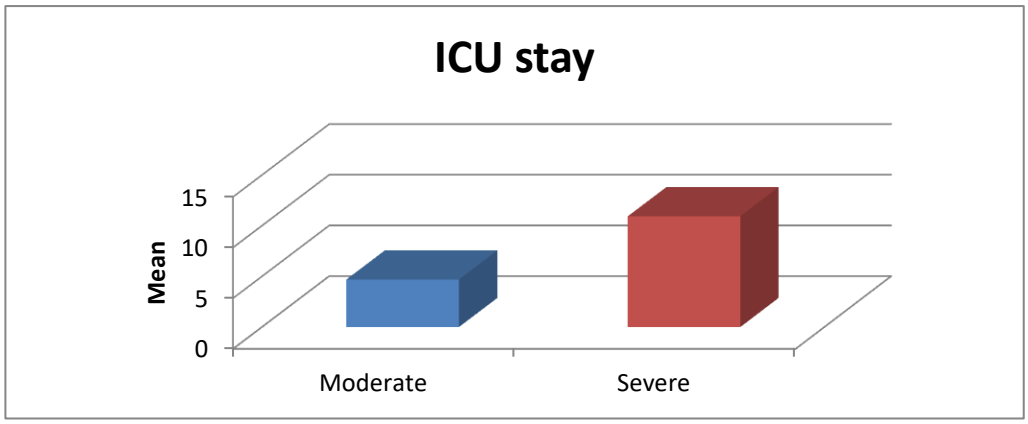

Figure 12: Mean ICU stay in moderate and severe traumatic brain injury.

Table 13: Mean RBS at admission, 24hours and 72 hours in moderate and severe traumatic brain injury.

	Moderate		Severe		t	p-value
	Mean	SD	Mean	SD		
RBS at admission	125.69	27.14	158.25	44.82	-3.452	**0.001**
RBS at 24 hours	120.97	23.18	134.14	30.84	-1.884	0.065
RBS at 72 hours	119.00	15.92	119.36	18.12	-0.081	0.936

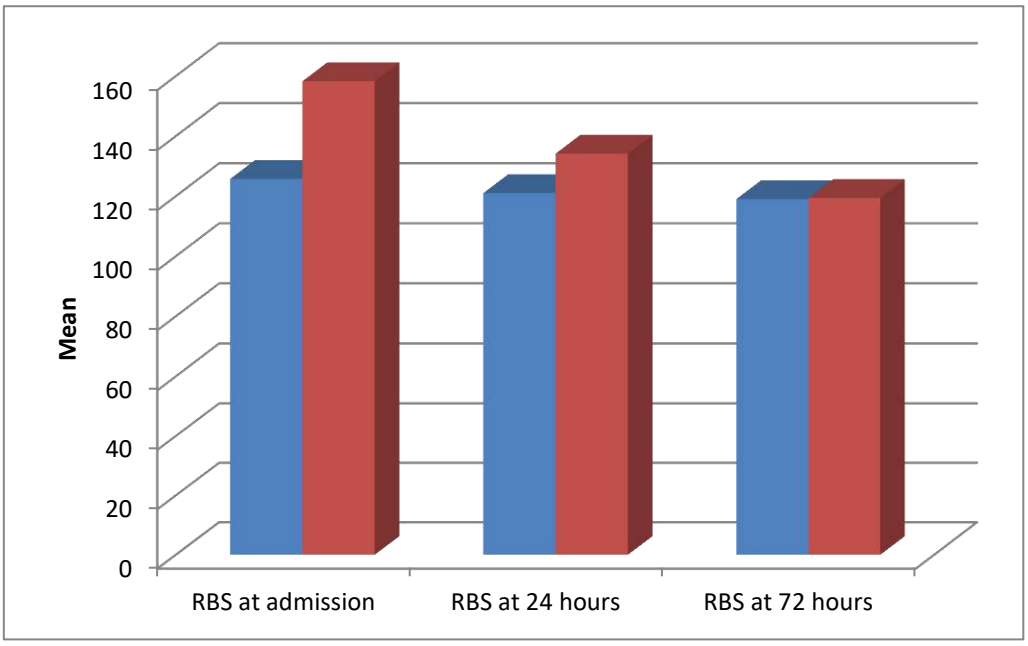

Figure 13: Mean RBS at admission, 24hours and 72 hours in moderate and severe traumatic brain injury.

DISCUSSION

The development of hyperglycemia itself might contribute to morbidity and mortality via generating a noxious cellular environment, causing electrolyte irregularities, and depressing immune efficacy. Clinical reports on trauma patients have mainly paid attention to patients with traumatic brain injuries in whom there is a positive association between blood glucose levels and mortality rates.In present study most of the patients were young adults, the Patients ranged from the age of 16 years to 68 years with the mean age being 34.63 ± 10.70 years for moderate and 35.54± 12.34 years for severe traumatic brain injury. It was seen that the majority of the patients in the moderate and severe TBI were in the age group of <40 years. Younger people were observed to be more prone to traumatic brain injury. A finding which has been replicated in the previous literature[81-83].In our study male patients out numbered female patients(6.5:1). Males were observed to be more prone for both moderate and severe traumatic brain injury. In study by Haron et al which included 294 patients ,the mean age of the study sample was 34.2 ±13.0 yrs and about 75% of the study participants were 43 years of age or younger. Of the 294 cases included in the study, 50 patients (17.0%) were females and 244 (83.0%) were males[82,83].

Road traffic accidents was the major reason of both moderate and severe TBI. The other reasons included assault, fall from height and unknown mechanisms. However, Alvis-Miranda HR et al reported that traffic accidents and assault were the more common cause of TBI followed by falls. Another Indian study by Saxena et al[84] revealed road traffic injuries as the leading cause (60%) of TBIs, followed by falls (20%-25%), and violence(10%).

In present study out of total 60 patients 46.67 % patients had severe traumatic brain injury and 53.33% of the patients had moderate traumatic brain injury. It was observed that severe TBI had raised sugar levels as compared to the moderate TBI, at all the three points of RBS measurements. Our finding is comparable to the evidence present

in literature[81,82]. Salehpoor et al [85] found that on review of 22 studies which investigated blood glucose levels as a prognostic factor all except three studies, reported that high levels of blood sugar is associated with poor prognosis. Takanashi et al.[86] looked retrospectively at the clinical course of patients with head injury, which have been grouped into various categories on admission. Patients with severe head injury had higher serum glucose levels, at 11.1 mmol/L compared with patients with moderate head injury, at 9.5 mmol/L. Walia et al[87] suggested that hyperglycaemia is more strongly predictive of the outcome of 338 patients with head injury as compared with mean arterial blood pressures. When both factors were included in a regression analysis, each factor was independently associated with mortality; however, there was a stronger relationship between blood glucose and mortality than between mean arterial blood pressure and mortality. It was found that ICU stay was increased in patients with hyperglycaemia in both moderate and severe head injury patients. A significant increase in ICU stay was found in the patients with severe head injury with increased blood glucose at admission. Neurological status was a better determinant for ICU stay than blood sugar levels during first 2 days of admission. Hospital stay also significantlyincrease in severe traumatic brain injury.

In this study, in moderate traumatic brain injury RBS levels with respect to Glasgow outcome scale was not found to be statistically significant. In severe traumatic brain injury RBS levels at 24 hours with respect to Glasgow outcome score was found to be statistically significant. Patients with RBS levels 126.00 ±19.06 mg/dl at 24 hours the time of presentation were found to have a good outcome. RBS levels at the time of admission and at 72 hours were not found to be statistically significant. While other studies have found RBS levels at the time of admission significant, they have not reported such significance in RBS levels at 24 hours. On the similar lines, current evidence in literature proposes that hyperglycemia is associated with poor outcomes, good outcome has been seen in patients in whom the difference in blood glucose levels at admission and 24 hours post-

surgery is <20 mg/dl. As per evidence, hyperglycaemia is significantly associated with higher rates of complications (p=0.019)and mortality(p=0.039). However, the actual cut off for RBS to be proven as a deterrent varies in literature i.e. > 187.0 mg/dl, ≥160 mg/dl and ≥200 mg/dl. The mechanisms of how glucose worsens the ischemic threshold in neurons after injury are not well understood.In neuron cultures exposed to ischemic conditions, post-ischemic superoxide production and cell death are prevented by removing glucose from the medium These studies suggest that glucose is a requisite electron donor for reperfusion-induced neuronal superoxide production[88]. It is also reported that presentation of the ischemic brain with high levels of glucose would drive anaerobic glycolysis, resulting in the accumulation of toxic levels of lactic acid[89]. Thus the neuronal damage that occurs after TBI due to oxidative stress, hypoxia induced apoptosis and neuro inflammation are potentiated by the neurotoxic effects of glucose. Lorenzi et al states that high glucose interferes with the regulation of cell cycle and brings about programmed cell death[90]. This explains the worse prognosis of TBI patients having hyperglycemia.

SUMMARY & CONCLUSION

Our study highlighted that the traumatic brain injury is more commonly seen in younger age group. Males are more frequently affected then female. The Glasgow coma scale was moderate in more than half of the patients. Road traffic accidents were the most common cause for traumatic brain injury. At all the time of presentation higher levels of random blood sugar (RBS) was found in patients with severe traumatic brain injury. The ICU stay in severe traumatic brain injury had a significant correlation with the random blood sugar (RBS) at admission, whereas in the moderate traumatic brain injury it was not found to be statistically significant. In severe traumatic brain injury random blood sugar levels at 24 hours of admission with respect to Glasgow outcome score was found to be statistically significant. This study accentuates the fact that hyperglycemia can and should be used more frequently as a biomarker for the outcome in traumatic brain injury, specially in a low and middle income countries such as ours, where there is a crunch of sophisticated lab investigations, regular monitoring of the random blood sugar(RBS) is sternly advisable.

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S.N.	MRD	Name	Age (yrs)	Sex	Hospital stay (days)	ICU stay (days)	RBS at admission (mg/dl)	RBS at 24 hours (mg/dl)	RBS at 72 hours (mg/dl)	TBI	Glasgow Outcome Scale	Mode of injury	HbA1c
1	1137132	YHS	48	M	8	3	104	110	108	Moderate	4	RSA	5.2
2	1125113	Ms	51	M	80	16	152	164	140	Severe	2	RSA	5.4
3	1142634	Ss	29	M	58	16	128	140	96	Severe	3	RSA	5.8
4	1181106	Dr	45	M	8	3	91	124	114	Moderate	5	assault	5.4
5	1122037	Vr	50	F	4	4	180	201	138	Severe	2	RSA	5.4
6	1113306	Ls	43	M	5	5	198	240	140	Severe	1	RSA	5.5
7	1123466	As	17	M	15	9	194	160	98	Severe	4	RSA	5
8	1178410	Vk	40	M	15	7	128	150	142	Severe	5	Assault	5.3
9	1143305	Gs	30	M	40	13	145	137	155	Severe	3	RSA	5.1
10	1172038	Ls	33	M	15	8	168	120	122	Moderate	5	RSA	5.3
11	1171822	Ls	25	M	14	2	109	91	110	Moderate	5	RSA	5.4
12	1171266	A	23	F	5	Nil	96	104	110	Moderate	5	RSA	5.2
13	1158312	Js	28	M	32	24	119	108	113	Severe	5	RSA	5.1
14	1149094	As	68	M	44	9	212	113	123	Severe	4	RSA	5.1
15	1176263	Ks	33	M	25	15	117	135	126	Moderate	4	RSA	5.1
16	1068853	Ak	26	M	5	Nil	110	98	116	Moderate	5	RSA	4.9
17	994150	Js	24	M	11	4	101	108	115	Moderate	5	RSA	4.9
18	1096189	Kt	31	F	15	7	121	182	128	Moderate	5	RSA	5.1
19	1112465	R	22	M	9	Nil	77	102	104	Moderate	5	RSA	5.6
20	965419	Jd	36	M	5	3	124	96	105	Moderate	5	RSA	5
21	1097607	Js	38	M	34	28	144	111	115	Severe	5	RSA	6
22	1167586	Ps	22	M	14	11	190	102	101	Severe	5	RSA	5.7
23	1168566	Gs	45	M	7	Nil	116	101	110	Moderate	5	RSA	4.9
24	538766	Js	32	M	13	6	134	101	95	Moderate	5	RSA	5
25	1163583	Bs	26	M	9	4	181	144	166	Severe	5	RSA	4.9
26	1153228	Js	41	M	27	7	123	122	132	Moderate	5	RSA	5.3
27	1180337	As	18	M	11	Nil	90	104	112	Moderate	5	RSA	5.1
28	1183284	Rs	27	M	10	Nil	108	124	116	Moderate	5	RSA	5
29	1175414	Hs	45	M	15	9	195	127	110	Severe	5	RSA	5.6
30	1176256	Jl	50	M	17	10	130	118	110	Moderate	5	RSA	5.7
31	1173657	Ak	45	F	20	12	112	110	142	Moderate	5	RSA	5.5
32	1174207	A	30	M	20	13	111	123	128	Moderate	5	RSA	4.9
33	107217	Kp	50	M	8	2	130	128	112	Moderate	5	RSA	5.1
34	1084316	Ng	47	F	9	6	160	130	98	Moderate	5	RSA	5.2
35	1080497	As	18	M	15	12	148	170	102	Severe	5	RSA	5.1
36	1094219	Ak	19	M	11	Nil	114	102	130	Moderate	5	RSA	4.9
37	1128943	Ck	32	M	6	3	90	116	104	Severe	5	Fall from height	5.1
38	1164802	Ns	22	M	9	3	141	116	104	Severe	5	RSA	4.9
39	1083637	Ms	36	M	34	13	275	134	115	Severe	2	RSA	5.2
40	1122031	Ms	27	M	34	5	132	102	91	Moderate	5	RSA	5
41	1131613	Mk	35	M	9	3	137	111	110	Moderate	5	RSA	5.1
42	1135143	Ns	36	M	11	Nil	87	116	120	Severe	4	RSA	5.6
43	1133945	S	16	F	9	6	270	114	108	Severe	5	Rail track accident	5
44	1065251	Gs	38	M	67	14	130	128	120	Severe	2	RSA	4.9
45	1135965	Vs	35	M	15	8	135	122	111	Severe	5	RSA	4.4
46	1109539	Ks	34	M	29	6	149	126	121	Severe	4	RSA	5.7
47	1105939	Pk	45	F	11	4	163	151	147	Moderate	5	Domestic fall	6
48	1113711	Mr	40	M	54	21	138	128	122	Severe	2	RSA	5.4
49	1114103	Mr	57	M	51	19	131	92	108	Severe	2	RSA	5.5
50	1091482	As	26	M	11	Nil	161	144	132	Moderate	5	RSA	5.3
51	958868	Bs	35	M	15	9	116	126	104	Severe	5	RSA	5.1
52	968130	K	22	M	25	19	135	114	118	Severe	4	RSA	5.2
53	1003575	Js	42	M	4	Nil	136	116	121	Moderate	5	RSA	5.1
54	1002346	Ks	42	M	10	7	170	132	104	Severe	5	RSA	4.8
55	1000603	Kc	60	M	11	3	190	126	120	Moderate	5	RSA	5.3
56	995694	Rk	45	M	21	11	150	125	144	Severe	4	RSA	4.9
57	1001524	Ss	26	M	11	2	140	126	108	Moderate	5	RSA	5.7
58	993813	Gk	30	M	23	10	184	196	124	Moderate	4	RSA	5.8
59	996856	Sk	25	M	17	9	133	141	162	Moderate	5	RSA	5.2
60	5933	Jk	42	F	18	13	100	125	150	Moderate	4	RSA	5.2

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Subject: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of Dr Manish Sharma, a student of your college for MCh Neuro-Surgery along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
To study random blood sugar level as a prognostic factor in moderate and severe traumatic brain injury

Supervisor
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The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

13. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

TO STUDY RANDOM BLOOD SUGAR LEVEL AS A PROGNOSTIC FACTOR IN MODERATE AND SEVERE TRAUMATIC BRAIN INJURY

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED
IN PARTIAL FULFILMENT OF THE REQUIREMENTS
FOR THE DEGREE OF

M.Ch.

In

NEUROSURGERY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES
FARIDKOT

MARCH, 2020

DR. MANISH SHARMA

DEPARTMENT OF NEUROSURGERY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
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ABSTRACT OF PLAN OF THESIS

Title	**TO STUDY RANDOM BLOOD SUGAR LEVEL AS A PROGNOSTIC FACTOR IN MODERATE AND SEVERE TRAUMATIC BRAIN INJURY**
For the degree of	**M.Ch. Neurosurgery**
Name of the candidate	**Dr. Manish Sharma**
Supervisor	**Dr. Ashwani K Chaudhary,** Professor, Department of Neurosurgery, DMCH, Ludhiana
Co-supervisor	**Dr. Shivender Sobti**, Associate Professor, Department of Neurosurgery, DMCH, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
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INTRODUCTION: Head trauma Is a major cause of death, disability and public health problems. Damage induced by TBI is divided into 2 types- (1- Primary injury is initiated by a physical insult to the head, resulting in compression and shearing of adjacent tissues, (2- Secondary injuries are complex process that occurs in the hours and days following primary injury, which encompass cranial and systemic complications. Cranial complication may include cerebral edema, intracranial HTN, infection, calcium ion toxicity and vasospasm. Systemic complication are mainly ischemic in nature, and include hypoxemia, hypotension, hypertension, hyperglycemia and hypoglycemia. Among these secondary complications, hyperglycemia in TBI pt is one of the most common, and correlate the severity of injury and clinical outcome.

AIMS & OBJECTIVES: To evaluate the role of random blood glucose levels as a prognostic factor in moderate and severe head injury patients, in non diabetic patients.

MATERIAL & METHOD: Consecutive sample of 60 pts admitted in department of neurosurgery, DMCH, Ludhiana as case of moderate to severe head injury be enrolled for prospective and observational study from March 2020 to September 2021. Glucose levels of the pts will be evaluated by collecting venous sample at admission at 24 hrs and at 72 hrs of stay patients pre-existing diabetic status will be ruled out by Glycosylated HB (HbA1c) levels.

CLINICAL SIGNIFICANCE: Blood sugar control in traumatic brain injury patients leads to faster restoration of consciousness and better outcomes.

KEYWORDS: Random Blood Sugar, Moderate Brain Injury, Severe Brain Injury, Glycosylated HB.

Manish Sharma — Shivender Sobti — A.K. Chaudhary — Principal

Candidate's sign Co- supervisor's sign Supervisor's sign Principal's sign

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"TO STUDY RANDOM BLOOD SUGAR LEVEL AS A PROGNOSTIC FACTOR IN MODERATE AND SEVERE TRAUMATIC BRAIN INJURY"** exist in the Department of Neurosurgery, Dayanand Medical College, Ludhiana & will be provided to the candidate. We will see that the data being included in the thesis are genuine & is collected by the candidate himself under our supervision & guidance.

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APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
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Topic of Thesis	TO STUDY RANDOM BLOOD SUGAR LEVEL AS A PROGNOSTIC FACTOR IN MODERATE AND SEVERE TRAUMATIC BRAIN INJURY
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PROFORMA FOR REGISTRATION OFSUBJECT FOR DISSERTATION

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2	NAME OF THE INSTITUTE	DMCH , LUDHIANA
3	COURSE OF STUDY AND SUBJECT	MCH NEUROSURGERY
4	DATE OF ADMISSION OF COURSE	11 SEPTEMBER 2019
5	TITLE OF THE TOPIC	TO STUDY RANDOM BLOOD SUGAR LEVEL AS A PROGNOSTIC FACTOR IN MODERATE AND SEVERE TRAUMATIC BRAIN INJURY

6 BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Head Trauma (HT) is a major source of death, disability and important public health problem in the world [1]. Injuries related to head trauma are the main cause of early deaths, conditions such as hypotension, hypoxia, increased intracranial pressure, and hyperglycaemia, can increase mortality.

Some researchers believe that critically ill patients with hyperglycaemia generally have a low Glasgow Coma Scale (GCS) score, increased complications and poor outcome [2].

On the other hand, some authors disagree on the association of hyperglycaemia and poor outcome in TBI and believe that high blood glucose levels are transient and generally reflect a metabolic response after injury [3].

Prevention and early treatment of these parameters that could lead to secondary injuries are considered to improve outcomes.

The hyperglycaemia has also been suggested to be transient and it is associated with severe head injury and poorer neurological outcome.[4]

The reasons for the poorer neurological outcome is not well understood but several investigators have postulated that brain injury is aggravated by elevated glucose levels because of enhanced anaerobic glycolysis and lactic acidosis in ischaemic conditions.[5]

Jeremitsky et al. study showed that early hyperglycaemia in severe trauma patients' associated with poor outcomes and tight glucose control is needed to achieve better outcomes and prognosis.[6]

Hyperglycaemia worsens cerebrospinal and renal damages since it cause ischemia (insufficient blood supply), hypophosphatemia (serum phosphate reduction), gastro paresis (delayed gastric emptying), delayed wound healing, and white blood cells dysfunctions.[7] The results of conducted survey showed that controlling blood sugar level in traumatic brain injury patients leads to faster restoration of consciousness and better outcomes.[6]

Blood glucose possesses all properties of an ideal serum marker of systemic injury. It is highly sensitive for cerebral cellular injury secondary to head trauma. Al-though the pathophysiology of hyperglycemia's neuro-pathic effect is not entirely clear, it has been reported that it aggravates ischemic acidosis, which in turn worsens brain edema. Cochran reported that blood glucose levels more than 300 mg/dl is associated with death.[8]

We need to evaluate the role of random blood glucose levels as a prognostic factor in moderate and severe head injury in non diabetic patients.

6.2 REVIEW OF LITERATURE

In a study by Kafaki et al about 39% (*n* = 85) of patients were admitted with hyperglycemia during the study period. The mortality rate in patients with glucose $200 mg/dL was 65.8% (*N* = 56), against 23.7% (*N* = 32) in the group with glucose, 200 mg/dL, with mortality rising as the blood glucose level increased (*P* = 0.014).[9]

In a study by Usha Adiga et al in 2012Random Blood Sugar (RBS) was 189.93 ± 51.74 mg/dl in patients and 106.47±18.32 mg/dl in healthy controls. Blood sugar is significantly elevated in TBI patients compared to controls (P<0.0001).GCS of patients ranged from 3-14. Correlation study showed that Glasgow coma scale bears a strong negative correlation(r= - 0.7043) with blood sugar which is statistically significant (p<0.05). This implies that higher the Random Blood Sugar, worse is the patient's status of consciousness and vice versa.[10]

In a study in 2015 by Javaher Khajavikhan et al about 34(40%) of patients were admitted with hyperglycaemia (RBS ≥ 200 mg/dl) over the study period. The mortality rate, length of ICU stay, hospital stay, ISS and VAP & ARDS in patients with RBS levels ≥ 200 mg was significantly higher than patients with RBS levels below ≤ 200mg (p<0.05, p<0.001). A significant correlation was found between RBS with GCS arrival, length of ICU stay, length of hospital stay, ISS, mechanical ventilation and VAP & ARDS (p<0.05, p< 0.001). RBS is a predicate factor for ISS (p <0.05, OR : 1.36), GCS (p <0.001, OR : 1.69), mechanical ventilation (p< 0.05, OR : 1.27), VAP & ARDS (p <0.001, OR : 1.68), length of ICU stay (p <0.001, OR : 1.87) and length of hospital stay (p <0.05, OR : 1.24).They concluded that hyperglycemia after severe TBI is associated with poor outcome. It can be predictive factor for mortality rate, icu stay, gcs arrival, VAP and RDS, hospital stay and ISS. Management of hyperglycemia with insulin protocol in cases with value more then 200 mg/dl, is critical in improving the outcome of pts with TBI.[11]

Adeolu, et al conducted a study in the Nigerian population in the year 2015 in which there were 146 male and 30 female patients (range: 2 years to 78 years; mean; 34.4 years, SD: 16.4 years). Most (36.4%) of the patients had severe HI. Only 2.5% of the patients had hyperglycaemia at admission. Death occurred in 25% of the patients, moderate disability occurred in 30.1% and good outcome occurred in 35.8%. Hyperglycaemia occurred in one patient each in mild and severe head injuries and in two patients withmoderate head injury. All the patients with hyperglycaemia had favourable outcomes.[12]

Danisman et al conducted a study in which the median age of the study population was 7 years and the median GCS was 11. There was a significant negative correlation between blood glucose level and GCS ($p < 0.05$). A significant correlation in the negative direction was observed between GCS and blood glucose level ($r = -0.658$, $p < 0.05$). Seventy-seven percent of the patients were admitted to hospital, while 6% died in ED.[13]

In a study by Torbati et al as the SCI tauma was more severe, the blood sugar level inceases with a higher rate. Besides, there was a significant difference ($p = 0.001$) in MF of patients before and after the insulin protocol prescriptionnneurosurgical patients is known to correlate highly with progression of prior imaging abnormalities and also new pathology. This has been demonstrated in unselected neurosurgical patients traumatic brain injury (TBI),vascular pathology, and in the postoperative period. When neurological deterioration is not verifiable—for example, as in the case of a patient with poor results on baseline examination or under sedation—the value of routine imaging has also been demonstrated, with detection of new pathology and worsening of preexisting findings.[14]

LiuDeRyke *et al.* demonstrated that peak random blood sugar within the first twenty four hours of injury and admission has the best prognostic value in predicting outcome.[15]

Miller et al., found the impact of severity of brain trauma on blood sugar increasing rate.[16]

Marton in children found that hyperglycemia with in the first 24 hrs of TBI was highly a/w poor outcome.[17]

Rovias et al., in the study on 267 pts with moderate or severe TBI demonstrated that the level of hyperglycemia were reliable predictors of severity and neurological damage.[18]

Shi et al. found that hyperglycemia(both peak glucose and persistent hyperglycemia) is one of the most common secondary complication of severe TBI and is associated with poor clinical outcomes after this type of injury.[19]

6.3 AIMS AND OBJECTIVES OF THE STUDY

To evaluate the role of random blood glucose levels as a prognostic factor in moderate and severe head injury in non diabetic patients.

7.0 MATERIALS AND METHODS

This study is a prospective study of all moderate and severe traumatic brain injuries admitted at Neurosurgery Department, DMCH during March 2020 to September 2021 time period. Glucose levels of the patients will be evaluated by collecting venous samples at admission, at 24 hrs and at 72 hrs of stay. Patients pre existing diabetic status will be ruled out by HbA1c levels. Data on mortality, ICU length of stay, hospital length of stay, admission GCS score, requirement of mechanical ventilation will be collected. Severity of head injury will be graded using Glasgow coma scale into mild (13-15), moderate (9-12) and severe (3-8).

7.1 SOURCE OF DATA

Sixty consecutive moderate and severe traumatic brain injury patients admitted at Neurosurgery Department, DMCH during March 2020 to September 2021 time period.

7.2 METHODS OF COLLECTION OF DATA

Inclusion Criterion-

- Sixty consecutive patients admitted as case of moderate or severe traumatic brain injury

Exclusion Criterion-

- Pre-existing diabetic status
- Pre- existing comorbidities.
- Pre-existing metabolic disorders like liver pathologies.
- Polytrauma patients

Duration of Study/ Number of Cases - March 2020 to September 2021, consecutive sample of 60 patients admitted as case of head injury be enrolled for study.

OUTCOME: Outcome will determined by Glasgow outcome score (1-5) at the time of discharge from the hospital

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. For comparing categorical data, Chi

square ($\chi 2$) test will be performed and exact test was used when the expected frequency is less than 5. A probability value (p value) less than 0.05 will be considered statistically significant. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

- Blood sugar monitoring on admission, 24 hrs and at 72 hrs of stay
- Glycosylated HB to rule out pre-existing diabetic status

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached Herewith

8. LIST OF REFERENCES

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PROFORMA

NAME

AGE

SEX

CR No

Date of Admission

Date of Discharge

Duration of hospital stay

Clinical History:

GENERAL EXAMINATION

GCS

VITALS

Pallor/Cyanosis/Clubbing/Icterus/edema/Lymphnode/ Neck Veins

CVS

RESPIRATORY SYSTEM

ABDOMINAL EXAMINATION

CNS EXAMINATION

	At admission	At 24 hours	At 72 hours
Age			
GCS			
Random blood glucose			
Length of hospital stay			
Length of icu stay			
Mechanical Ventilation			

GLASGOW OUTCOME SCORE

5 (good outcome)		
4 (Moderately disabled)		
3 (severely disabled)		
2 (persistent vegetative sate)		
1 (Death)		

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o..... am willing to participate in the study **"TO STUDY RANDOM BLOOD SUGAR LEVEL AS A PROGNOSTIC FACTOR IN MODERATE AND SEVERE TRAUMATIC BRAIN INJURY"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out of the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____ इस शोधकार्य **"TO STUDY RANDOM BLOOD SUGAR LEVEL AS A PROGNOSTIC FACTOR IN MODERATE AND SEVERE TRAUMATIC BRAIN INJURY"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"TO STUDY RANDOM BLOOD SUGAR LEVEL AS A PROGNOSTIC FACTOR IN MODERATE AND SEVERE TRAUMATIC BRAIN INJURY" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ

_____ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____

ਪਤਾ _____

ਮਿਤੀ_____

ਪਤਾ _____

_____ ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____ ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ